



## Studies on hypoglycaemic and wound healing activities of *Lantana camara* Linn.

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### Abstract

**Objective:** To study the antihyperglycaemic and wound healing activity of the leaf extracts of *Lantana camara* Linn. on rats. **Materials and methods:** Antihyperglycaemic activity of the aqueous extract of the leaves was evaluated by using both normoglycaemic and alloxan induced hyperglycaemic rats. The wound healing activity was assessed for both leaf juice and hydroalcoholic (ethanol 50% v/v) extract of the leaves on excised rats. **Results:** The aqueous extract was found to produce significant reduction of blood glucose concentration between 2-4 h of administration in alloxan induced hyperglycaemic rats at tested dose levels. However, in normoglycaemic animals, the extract at 400mg/kg produced significant reduction of blood glucose between 2-4 h of administration. In the wound healing studies, the leaf juice was found to be more active than the extract. **Conclusion:** In the light of the alarming toxicity of the plant, the use of this plant in whole or any part there of need to be carefully regulated until the toxic principles of the plant are identified and removed, to ensure a safe and effective treatment for diabetes.

**Key words:** *Lantana camara* Linn., *Kondh* tribes, Alloxan, Antihyperglycaemic, Wound healing.

### 1. Introduction

*Lantana camara* Linn. (Fam-Verbenaceae) is a large scrambling evergreen shrub, a native of tropical America and completely naturalised in many parts of India as an ornamental plant. The plant finds its application in various folklore medicines for a variety of ailments around the globe. The popular use of the plant, however mainly refers to its abortifacient, antimalarial,

antiinflammatory, emmenagogue, antitussive, antipyretic, antiulcer and wound healing property [1-3].

The leaves of the plant are reported to be used as appetiser [4], aphrodisiac [5], antimalarial [6], jaundice, analgesic and antiinflammatory [7] and in the treatment of wounds, ulcers, bruises, sores and infections of skin and mucosa [8].

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The leaves in the form of decoction are also reported to be useful in treating diabetes by the tribes of Tonga and Trinidad [9]. Even the kondh tribes of Dhenkanal district of Orissa use the leaves of the plant as a traditional medicine for the treatment of diabetes in the form of hot aqueous extract (decoction).

An extensive search of the literature reveals no reports on the antihyperglycaemic and wound healing activity of the plant. However, the reports reveal that the leaves cause a number of toxic effects like nephrotoxicity, hepatotoxicity, photosensitization, dermatitis, intestinal haemorrhage and paralysis of the gall bladder [10, 11]. The vast ethnomedical use of the plant around the globe for the treatment of various diseases and ailments triggered this research investigation to study the antihyperglycaemic and wound healing property of the leaves.

## 2. Materials and Methods

### 2.1 Plant material

Fresh leaves were collected during early summer from young matured plants from the rural belt of Salipur in Cuttack district of Orissa after identifying the plant by the botanists of Ravenshaw College, Cuttack; by comparing with the voucher specimen present in the herbarium. The collected leaves, after washing under running tap water were dried under shade, pulverised, passed through sieve no. 40 and used for further studies. A specimen of the plant species is deposited in the Department of Pharmacognosy of the institute for future reference.

### 2.2 Preparation of extract

The powdered leaves were extracted separately with distilled water by decoction for 10 min and with ethanol-water (1:1) by maceration for 72 h. The liquid extracts were concentrated under vacuum to yield dry extracts (aqueous

extract yield 18.14% w/w and hydroalcoholic extract 11.47% w/w with respect to dry material) and preserved in a desiccator till further experiments. The aqueous extract was dissolved in 0.5% w/v sodium carboxymethyl cellulose in distilled water and used for the antidiabetic screening. Whereas the hydroalcoholic extract and fresh leaf-juice (obtained by expression of fresh leaves) incorporated in simple ointment I.P were used for the wound healing study.

### 2.3 Animals used

Adult wistar albino rats (150-200g) of either sex were used in the studies. The animals were kept in standard polypropylene cages at room temperature of  $30 \pm 2^\circ\text{C}$  and 60-65% relative humidity.

## 3. Experimental

### 3.1 Antidiabetic evaluation [12,13]

#### 3.1.1. Using hyperglycaemic rats

The acclimatized animals were kept fasting for 24 h with water *ad libitum* and injected intraperitoneally a dose of 120 mg/kg of alloxan monohydrate in normal saline. After one hour, the animals were provided feed *ad libitum*. The blood glucose level was checked before alloxanisation and 24 h after alloxanisation by withdrawing blood from the tip of the tail of each rat under mild ether anaesthesia. The blood glucose level was measured with haemoglucostrips supplied by M/s Pulsatum health care Pvt. Ltd., Bangalore with the help of a Pulsatum blood glucose monitor.

Animals were considered diabetic when the blood glucose level was raised beyond 200mg/dl of blood. This condition was observed at the end of 48 h after alloxanisation. The animals were segregated into four groups of six rats in each. Group-I served as negative control and received vehicle (2 ml/kg) through oral route. Group-II received glibenclamide

(2.5mg/kg). Group-III and IV received the aqueous extract at doses of 200 and 400 mg/kg in a similar manner. Blood samples were collected from each rat by cutting the tip of the tail under mild ether anaesthesia. Blood glucose level was estimated at 0, 1, 2, 4 and 8 h respectively.

### 3.1.2. Using normoglycaemic rats

The animals were fasted for 18 h, but were allowed free access to water before and throughout the duration of experiment. At the end of the fasting period, taken as zero time (0h), blood was withdrawn from the tip of the tail of each rat under mild ether anaesthesia and the blood glucose was estimated as above.

The normal rats were then divided into three groups of six animals each Group I served as negative control to which the vehicle (0.5% w/v sodium CMC) was administered through oral route. Group II received glibenclamide (2.5 mg/kg) and served as reference control, Group III and IV received the aqueous extract at doses of 200 and 400 mg/kg in a similar manner. Blood glucose levels were monitored after 1, 2, 4 and 8 h of administration of single dose of test samples.

### 3.2. Wound healing evaluation (Excision wound model) [14]

The selected animals were divided into four groups of six in each. All the test samples were applied topically.

The hair on the skin of back surface of animals were removed by using a suitable depilatory (Anne French hair removing cream). Light incisions were made on the cleared surface by cutting the skin of the animals under mild ether anaesthesia. The area of the wounds were measured (sq. mm) immediately by placing a transparent polythene graph paper over the wound and then tracing the area of the wound on it.

This was taken as the initial wound area reading. Group-I served as negative control to which no treatment was given. Group-II served as positive control to which nitrofurazone (0.2 % w/w in simple ointment) was applied topically. Group III animals were treated with hydroalcoholic extract (10 % w/w in simple ointment) and Group-IV animals were treated with the juice of the fresh leaves in a similar manner. All the test samples were applied twice daily.

The wound area of each animal was measured on 1<sup>st</sup>, 4<sup>th</sup>, 8<sup>th</sup>, 11<sup>th</sup> and 14<sup>th</sup> day. The percentage healing was calculated from the days of measurements of wound area.

### 3.3 Statistical analysis.

Results were analysed by student's *t* - test. The minimum level of significance was fixed at  $P < 0.01$ .

## 4. Results and discussion

The studies on the aqueous leaf extract of the plant *L.camara* Linn. revealed that the extract caused significant reduction in the blood glucose levels in the rats. The extract was found to produce marked reduction in blood glucose concentration between 2-4 h of administration in alloxan induced hyperglycaemic rats at tested dose levels as depicted in table no.1.

However, in normoglycaemic animals, the extract at 400mg/kg dose level produced marked reduction of blood glucose between 2-4 h of administration (as reflected from table no.2). When compared with the reference control glibenclamide, the extract caused noticeable reduction in the blood glucose level in both classes of animals except that the onset of action of glibenclamide was noticed from the first one hour while that of the extract was from the 2<sup>nd</sup> hour at a dose level of 400mg/kg.

The comparable effect of the extract with glibenclamide may suggest similar mode of

Table No. 1. Effect of aqueous extract of the leaves of *L.camara* Linn. on the blood glucose concentration in alloxan induced hyperglycaemic rats.

Group	Treatment	Dose	Blood glucose conc. (mg/dl.)				
			0h	1h	2h	4h	8h
I	0.5% w/v Sodium CMC (Vehicle)	2 ml/kg	265.5 ± 11.92	271.83 ± 11.6	275.83 ± 11.47	282.17 ± 11.26	290.83 ± 9.86
II	Glibenclamide	2.5 mg/kg	289.67 ± 22.11	198.17 ± 16.7*	134.83 ± 9.94**	83.17 ± 2.89**	79.0 ± 2.2**
III	Aqueous extract	200 mg/kg	256.3 ± 13.81	221.38 ± 11.52	189.36 ± 16.34*	172.29 ± 15.12*	158.86 ± 9.86**
IV	Aqueous extract	400 mg/kg	278.85 ± 18.17	232.65 ± 16.47	176.46 ± 14.28*	132.28 ± 11.26**	101.76 ± 8.38**

Results expressed as Mean ± SEM from six observations; \* P < 0.01; \*\* P < 0.001

Table No. 2.

Effect of aqueous extract of the leaves of *L.camara* Linn. on the blood glucose concentration in normoglycaemic rats.

Group	Treatment	Dose	Blood glucose conc. (mg/dl.)				
			0h	1h	2h	4h	8h
I	0.5% w/v Sodium CMC (Vehicle)	2 ml/kg	96.17 ± 3.14	98.0 ± 3.66	97.17 ± 2.65	96.17 ± 2.06	97.24 ± 2.11
II	Glibenclamide	2.5 mg/kg	98.67 ± 3.6	82.67 ± 2.76*	73.33 ± 2.56**	64.5 ± 1.29**	62.17 ± 0.68**
III	Aqueous extract	200 mg/kg	92.13 ± 3.8	90.54 ± 3.26	88.12 ± 2.78	81.67 ± 2.64*	79.36 ± 1.79**
IV	Aqueous extract	400 mg/kg	88.48 ± 3.86	83.19 ± 3.43	78.68 ± 3.27*	69.27 ± 2.14**	64.98 ± 1.83**

Results expressed as Mean ± SEM from six observations; \* P < 0.01; \*\* P < 0.001

Table No. 3.

Effect of *L.camara* Linn. leaves on wound healing in excised rats.

Group	Treatment	Percentage inhibition of wound on the day of study				
		1 st	4 th	8 th	11 th	14 th
I	Control	0	19.28 ± 3.28	46.85 ± 5.97	55.26 ± 2.38	63.83 ± 1.18
II	Nitrofurazone (0.2% w/w)	0	24.79 ± 7.74	57.37 ± 7.38	86.74 ± 0.71	95.19 ± 0.32*
III	Hydroalcoholic extract (10% w/w)	0	20.5 ± 5.79	47.46 ± 4.98	72.18 ± 2.92	87.13 ± 1.27*
IV	Leaf juice	0	22.56 ± 6.59	56.23 ± 6.45	83.36 ± 1.82	94.19 ± 0.46*

Results expressed as Mean ± SEM from six observations; \* P < 0.001 on 14th day of study.

action, since alloxan permanently destroys the pancreatic  $\beta$ -cells and the extract lowered blood sugar level in alloxanized rats, indicating that the extract possesses extrapancreatic effects. The exact biological active constituent(s) responsible for the said effect are neither reported nor the exact mode of action of the hypoglycaemic activity was reported earlier, with the lone observation that it is used in folklore diabetic treatments.

The studies on wound healing activity reveals that all the four groups showed decreased wound area from day to day. However, on 14<sup>th</sup> day, Group-I animals showed 63.83% of healing (which may be due to self immunity of the animals) where as nitrofurazone treated animals showed 95.19% healing. On the other hand, the extract treated group showed 87.13% healing and the leaf juice treated groups exhibited 94.32% wound healing, as reflected in table no.3.

The present studies on hypoglycaemic and wound healing activities of *Lantana camara* Linn. leaves reveal that the extracts of the leaves showed significant antihyperglycaemic and wound healing activity, when compared with the controls. However, the literature received at hand proves the plant and its leaves are toxic in nature. The reported toxicities include weakness, anorexia, constipation, depression,

photosensitization, obstructive jaundice, dermatitis, liver and kidney damage, intestinal haemorrhage, paralysis of gall bladder and several other hepatotoxicities [10, 11]. However, the plant is reported to possess a number of therapeutic activities like analgesic, CNS depressant, smooth muscle relaxant, hypothermic, anticonvulsant, insect sex attractant, antifungal, antibacterial and antiyeast activities [10, 11, 15].

In the context of the long term therapeutic monitoring requirement for diabetes, and in the light of the alarming reports of its toxicity, the use of this plant in whole or any part there of need to be carefully regulated until the alarming toxic principles of the plant are properly identified and removed to ensure a safe and effective treatment for diabetes.

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